

REMARKS

Claims 1-9, 10, 11 and 25-34 are pending in the application. Claim 1 has been amended. Support for the amendment “wherein said targeted oligonucleotide construct has essentially no ability to cross the blood/brain barrier” may be found at page 46, last paragraph of the specification.

No new matter has been added by the present amendments. The amendments are being made not only to point out with particularity and to claim the present invention, but also to expedite prosecution of the present application. Applicants reserve the option to prosecute the pending claims further, or other ones, in the instant or a subsequent patent application.

Applicants thank Examiner for removing the rejections in the last Office Action.

CLAIM REJECTIONS

Rejection of claims under 35 U.S.C. § 102(b) over Kobori et al. and Pardridge et al.

The Examiner has rejected claims 1, 4, 5, 8, 11, 25-28, 30-32 and 34 over Kobori et al. (NeuroReport 1999 vol. 10, pages 2971-2974) and claims 1, 4, 5, 8, 10, 11, 25, 26, 28, 30, 31 and 34 over Pardridge et al. (Proc. Natl. Acad. Sci. USA 1995, vol. 92, pages 5592-5596).

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Both of the applied references describe constructs that have the ability to cross the blood/brain barrier. Applicants respectfully draw Examiner’s attention to page 46 of the specification, which details how the constructs disclosed in the instant specification did not show any appreciable ability to cross the blood/brain barrier. Applicants have amended claim 1 to clarify this property of the constructs. The remaining rejected claims are dependent from claim 1. Therefore, the instantly claimed invention is not anticipated by either the Kobori or the Pardridge reference. Applicants respectfully request reconsideration and withdrawal of the present rejections.

Rejection of claims under 35 U.S.C. § 103(a) over primary reference Kobori et al.

The Examiner has rejected claims 1, 4, 5, 8, 11, 25-28, 30-32 and 34 as obvious over Kobori et al. (NeuroReport 1999 vol. 10, pages 2971-2974) and claims 1, 4, 5, 9, 11 and 25-34 over Kobori et al. in view of Gewirtz et al. (U.S. 5,098,890) and Low et al. (U.S. 5,994,320).

To establish a *prima facie* case of obviousness, it is necessary for the Examiner to present evidence, preferably in the form of some teaching, suggestion, incentive or inference in the applied references, or in the form of generally available knowledge, that one having ordinary skill in the art would have been motivated to make the claimed invention and would have had a reasonable expectation of success in making the claimed invention. Under section 103, "[b]oth the suggestion and the expectation of success must be founded in the prior art, not in applicant's disclosure" (*Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.* 927 F.2d 1200, 1207, 18 USPQ2d 1016 (Fed. Cir. 1991), quoting *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed Cir. 1988)). Moreover, when a combination of references are used to establish a *prima facie* case of obviousness, the Examiner must present evidence that one having ordinary skill in the art would have been motivated to combine the teachings in the applied references in the proposed manner to arrive at the claimed invention. See, e.g., *Carella v. Starlight Archery*, 804 F.2d 135, 231 USPQ 644 (Fed. Cir. 1986); and *Ashland Oil, Inc. v. Delta Resins and Refractories, Inc.*, 776 F.2d 281, 227 USPQ 657 (Fed. Cir. 1985). Finally, the prior art reference (or references when combined) must teach or suggest all of the claim limitations (M.P.E.P. 2143).

The Examiner has not set forth any motivation to combine these references and hence has not established a *prima facie* case of obviousness. Moreover, even if there were motivation to combine the references, the combination does not teach or suggest each and every element of the claims.

Specifically, the Examiner has rejected claims 1, 4, 5, 9, 11 and 25-34 over Kobori et al. in view of Gewirtz et al. (U.S. 5,098,890) and Low et al. (U.S. 5,994,320). As discussed above, Kobori et al. describes constructs that have the ability to cross the blood/brain barrier. The instantly claimed constructs have little, if no, ability to cross the blood/brain barrier. Gerwitz et al. and Low et al. do not teach or suggest how the constructs of Kobori may be modified so that they do not cross the blood/brain barrier. Accordingly, the combination does not teach or

suggest each and every element of the claims, and the Examiner has not established a *prima facie* case of obviousness using these references.

Further, the Examiner has rejected claims 1, 4, 5, 8, 11, 25-28, 30-32 and 34 as obvious over Kobori et al. (NeuroReport 1999 vol. 10, pages 2971-2974). As discussed above, Kobori et al. describes constructs that have the ability to cross the blood/brain barrier. The instantly claimed constructs have little, if no, ability to cross the blood/brain barrier. One of skill in the art would not be motivated to modify Kobori to produce a construct that exhibits a *reduced* ability to cross the blood/brain barrier, because the blood/brain barrier strictly limits the ability of most agents to cross from the blood to the brain and very few effective delivery systems exist for the delivery of therapeutic molecules across this barrier. Accordingly, one of skill in the art would not be motivated to so modify Kobori in view of the art.

Applicants respectfully request reconsideration and withdrawal of the present rejections.

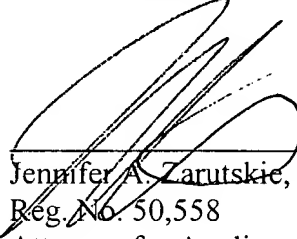
CONCLUSION

For the foregoing reasons, Applicants respectfully request reconsideration and withdrawal of the pending rejections. Applicants believe that the claims now pending are in condition for allowance, and notification of such is respectfully requested.

If, for any reason, a telephonic conference with the Applicants would be helpful in expediting prosecution of the instant application, the Examiner is invited to call Applicants' Agent at the telephone number provided below.

Respectfully submitted,

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